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RESEARCH PAPER

A prospective analysis examining frailty remission and the association with future falls risk in older adults in England

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Abstract

Background:Previous research has shown older adults experience dynamic changes in frailty status. This study aimed to determine the occurrence of sustained frailty remission and how remission is associated with falls risk.
Methods: Participants who contributed data to the analysis were in the English Longitudinal Study of Ageing from Waves 1 to 8 (2002–2017). Frailty was defined across waves using the frailty index and categorised into robust, pre-frail and frail. We classified participants who improved their frailty category from Wave 1 (2002) to Wave 2 (2004) and sustained/improved category again into Wave 3 (2006) and compared them with those who were either robust or frail across Waves 1–3. Cox proportional hazard modelling was used to determine the risk of incident falls reported at Waves 4–8, with results expressed as hazard ratios and 95% confidence intervals.
Results: Of 2,564 participants, 389 (15·2%) improved frailty category and sustained this during Waves 2–3, 1,489 (58·1%) remained robust and 686 (26·8%) remained frail during Waves 1–3. During the 10-year period (Waves 4–8), a total of 549 participants reported a fall. Compared with those who remained frail during Waves 1–3, those who with sustained frailty remission had a lower risk of future falls (HR 0·41; 95% CI = 0·36–0·45).
Conclusions: Frailty remission is possible and can be sustained across 5 years. There is a lower risk of future falls in those who sustain frailty remission compared with those who remain frail.

Keywords: frailty remission, falls risk, older adult, older people

Key Points

- Sustained frailty remission is possible.
- Sustained frailty is associated with a low risk of future falls compared with individuals with persistent frailty.
- This is the first study using the frailty index to assess sustained frailty remission over a 5-year period.

Research in context

Evidence before this study

Frailty is associated with an increased risk of falls, hospitalisation and mortality. Previous studies show that older adults experience dynamic changes in and may improve their frailty status. We searched Medline OVID plus additional reading lists with the search terms 'frail', 'frailty', 'older adult', 'elderly', 'transition', 'remission' with no language restrictions, from 1 January 2000 until 1 March 2021. We found limited data assessing sustained frailty remission and its association with future falls risk.

Added value of this study

To our knowledge, this is the first study using the frailty index to assess sustained frailty remission over a 5-year period and to determine the association between frailty remission and risk of future falls.

Implications of all the available evidence

Sustained frailty remission is possible and is associated with a lower risk of future falls compared with individuals with persistent frailty. This was of similar level of falls to that of robust individuals.

Introduction

Frailty is a state of increased susceptibility to adverse health outcomes and affects approximately a quarter of those aged 50 years and above with two main clinical tools used to assess it, the frailty index and frailty phenotype [1–4].

Previous research has shown frailty is associated with multiple adverse outcomes including an increased risk of hospitalisation, disability and mortality [5–7]. Frailty is associated also with an increased risk of falls, and frail individuals are more likely to experience recurrent falls. Pre-frail individuals also have an increased risk of falls [8]. Falls are a significant health problem in older people. Up to 20% of people who fall suffer injuries that reduce mobility and independence and 3% of falls in adults aged 65 years and above results in hospitalisation [9]. Further, most age-related limb fractures occur as the result of a fall with the risk of fracture often increased because of pre-existing co-morbidities including bone fragility and impaired neurophysiological responses.

With the demographic shift towards a more ageing population in most western countries, the prevalence of frailty is set to increase with consequent impact on health and social care [10]. It is important therefore to understand patterns, trends and associations within frailty, to advise public health interventions and service provision.

Frailty has been described as a transitional state in which individuals decline from robust to a state of reduced functional ability with an identified prodromal state of pre-frailty [11]. There has been research, however, to suggest that despite the idea of decreasing reserve, due to multiple factors comprising frailty, it may be reversed [11, 12].

Various interventions which have been trialled in frail groups show improvements in frailty status following intervention, e.g. exercise and physical reconditioning following a stressful event [11]. However, there are limited data that investigate transition states and trajectories of frailty in older adults over time, showing whether improvements can be sustained [12]. Kojima and colleagues performed a systematic review of studies assessing frailty remission and showed that 14% of people improved, 29% worsened and 57% maintained their frailty status over 3.9 years [13]. Similarly, Ofori-Asenso and colleagues reported that 23.3% of individuals transitioned from pre-frail to robust and 35.2% from frail to pre-frail or robust over a period of 3 years [14]. These studies, however, pooled remission rates from studies assessing transition at two given time points only. Data from a longitudinal study reported that older adults make frequent changes in frailty state over multiple time points and that sustained improvement is possible, whereas another cohort study produced a transition model to measure changes in frailty status [15, 16]. Although it might be expected that improvements in frailty status may translate into improved outcomes ,there is limited research assessing this.

Using data from the English Longitudinal Study of Ageing, a population survey of older men and women, we looked at change in frailty status at three time points over a 5-year period and investigated whether change in frailty status and in particular sustained frailty remission was associated with an observed lower risk of falls.

Methods

Study design and participants

We used participants aged 50 years and above from the English Longitudinal Study of Ageing (ELSA) representative of those living in England [17]. Data were collected by the National Centre for Social Research. The first wave of data collection began on 1 March 2002 with data collected every 2 years using computer-assisted personal interviews and self-completion questionnaires, and every 4 years using a nurse visit. There were also refreshment samples from the Health Survey for England with differing age criteria to correct for the age profile (Wave 3: 50–52 years; Wave 4: 50–74 years, Wave 6: 50–55 years and Wave 7: 50–51 years) [17]. Our study included 2,564 respondents who attend Waves 1, 2 and 3.

Assessment

Frailty

Frailty was assessed using Rockwood's cumulative deficit model. We produced an FI using deficits available from ELSA including 59 functional and psychological deficits (see Supplementary Table 1) [18]. We did not include falls in the

FI construct despite it being used in a previously published FI as it is the outcome variable for this study [19]. Binary variables were coded as '0' and '1' and distribution was used for ordinal/continuous variables. We coded '1' for variables that were irreversible across waves (e.g. Parkinson's disease). We summed each participant's deficits and divided them by a total possible to produce an index ranging between 0 and 1, in which higher scores indicated greater frailty. Frailty was categorised into pre-defined groups: robust (FI $\leq$ 0·08), pre-frail (FI $>$ 0·08 to $<$ 0·25) and frail (FI $\geq$ 0·25) [20].

For the main analysis, we identified three groups based on their frailty status in Waves 1, 2 and 3: sustained frailty remission, remain robust and remain frail (Supplementary Table 2). Respondents were classified as having sustained frailty remission if they improved their frailty status from Wave 1 to Wave 2 (frail to pre-frail, frail to robust and pre-frail to robust) and were able to sustain an improvement/improve further into Wave 3 (5 years after the Wave 1 visit). We categorised respondents as either 'remain robust' or 'remain frail' if their frailty status was assessed consistently as robust or frail, respectively, over the three waves.

As a sensitivity analysis, we looked at three further groups incorporating the remaining participants: remain pre-frail, frailty remission from Wave 2 to Wave 3 and frailty decline from Wave 2 to Wave 3. The respondents were categorised as 'remain pre-frail' if they were consistently pre-frail over the three waves, 'frailty remission from wave 2 to wave 3' if their frailty status improved from frail to pre-frail, frail to robust and pre-frail to robust between those two waves and 'frailty decline from wave 2 to wave 3' if their frailty status worsened from robust to pre-frail or frail, or from pre-frail to frail between those two waves.

Falls

Falls were assessed over a 10-year period using self-completed questionnaires that participants completed at subsequent study waves (Waves 4– 8). At each wave, participants were asked 'have you fallen down in the last two years (for any reason)?' Participants were coded as having experienced a fall if they responded yes to this question.

Covariates

We included sociodemographic and health behaviour variables associated with falls found from within the literature as covariates: age, ethnicity, gender, marital status, smoking behaviour and wealth [21–23]. Age was treated as a continuous variable. Ethnicity was categorised as Caucasian (all white self-reported ethnicities) or 'other' ethnicity (all self-reported mixed ethnic, Black, Black British, Asian, Asian British and any other group). We classified marital status as single, married, divorced or widowed. The analysis included smoking behaviour as an indicator of health behaviour; respondents were categorised as non-smokers, past smokers and current smokers. Wealth was assessed using the aggregate of private pension wealth and state pension wealth as presented as quintiles of wealth.

Statistical analysis

We used descriptive statistics to characterise participant characteristics including mean ± standard deviation for continuous data and frequency and percent for categorical data. Differences in characteristics between participants who had sustained frailty remission, remained robust and remained frail during Waves 1–3 were compared using chi-square tests for categorical variables and Kruskal–Wallis one-way analysis of variance for continuous variables.

The multivariate association between falls risk (outcome) and frailty status categories was assessed using Cox proportional hazard model with study wave used as the timescale. We modelled the risk of developing a fall for each of the three groups with sustained frailty as the reference group. Participants were censored for the wave in which a fall first occurred from Wave 4 onwards, drop out or Wave 8 or whichever end point came first. In the analysis, adjustments were made for the age, gender, marital status, smoking behaviour and wealth.

We performed a sensitivity analysis adding the remaining participants who joined Waves 1, 2 and 3. We divided the remaining participants into three groups (as outlined earlier): remain pre-frail, frailty remission from Wave 2 to Wave 3, and frailty decline from Wave 2 to Wave 3. We then repeated the analysis including these additional categories using the model described above. Data were analysed using STATA version 15.

Results

Baseline characteristics

The study sample consisted of 2,564 participants (1,208 male and 1,356 female) (see Table 1). At baseline, the average age of participants was 66·3 years (SD 9·5) and most participants (98·4%) were Caucasian. Of the 2,564 participants, 66.7% were married and 14.2% were current smokers. The mean frailty index was 0·1 (SD 0.2).

In total 389 participants (15.2%) improved frailty status from Wave 1 to Wave 2 and sustained/improved again into Wave 3, 1,489 (58·1%) remained robust and 686 (26·8%) remained frail across three waves.

Those who remained robust were younger (63.2 years) and had a lower FI (0.04) compared with those who remained frail (72.6 years and 0.4, respectively) and those who sustained frailty remission (66.7 years and 0.1 respectively). Those who sustained their frailty group or were frail were more likely to be female whereas those who remained robust were more likely to be male. Robust individuals or those who sustained frailty remission were more likely to Caucasian than from another ethnicity. Widowed individuals had approximately a double chance of being in the frail group compared with singles. Robust individuals were more likely to be non-smokers whereas those who were frail were more likely to be current smokers.

Table 1. Baseline characteristics of participants who improved and sustained their frailty group and those who were either robust or frail across three waves

	Total	Sustained frailty remission	Remain robust	Remain frail	
	N = 2,564	*N* = 389	*N* = 1,489	*N* = 686	*P*-value
Age, mean (SD)	66.3	66.7	63.2	72.6	<0.000
	(9.5)	(9.3)	(7.2)	(11.0)	
Frailty index, mean (SD)	0.1	0.1	0.04	0.4	
	(0.2)	(0.1)	(0.01)	(0.1)	
Gender	1,208	157	803	248	<0.000
Male, *n* (%)	(47.1)	(13.0)	(66.5)	(20.5)	
Female, *n* (%)	1,356	232	686	438	
	(52.9)	(17.1)	(50.6)	(32.3)	
Ethnicity					0.001
Caucasian, *n* (%)	2,524	386	1,473	665	
	(98.4)	(15.3)	(58.4)	(26.3)	
Other, *n* (%)	40	3	16	21	
	(1.6)	(7.5)	(40.0)	(52.5)	
Marital status					<0.000
Single, *n* (%)	125	20	71	34	
	(4.9)	(16.0)	(56.8)	(27.2)	
Married, *n* (%)	1,710	245	1,145	320	
	(66.7)	(14.3)	(67.0)	(18.7)	
Divorced, *n* (%)	299	54	147	98	
	(11.7)	(18.1)	(49.2)	(32.8)	
Widowed, *n* (%)	430	70	126	234	
	(16.8)	(16.3)	(29.3)	(54.4)	
Smoker status					<0.000
Non-smoker, *n* (%)	888	142	571	175	
	(34.6)	(16.0)	(64.3)	(19.7)	
Past smoker, *n* (%)	1,312	195	753	364	
	(51.2)	(14.9)	(57.4)	(27.7)	
Current smoker, *n* (%)	364	52	165	147	
	(14.2)	(14.3)	(45.3)	(40.4)	
Wealth quintiles					<0.000
1st	454	73	138	243	
	(18.1)	(16.1)	(30.4)	(53.5)	
2nd	445	62	180	203	
	(17.8)	(13.9)	(40.4)	(45.6)	
3rd	473	89	279	105	
	(18.9)	(18.8)	(58.9)	(22.2)	
4th	527	85	366	76	
	(16.1)	(22.0)	(69.4)	(14.4)	
5th	608	77	492	39	
	(24.3)	(12.7)	(80.9)	(6.4)	

Association between frailty group and risk of developing future falls

During 10 years of follow-up, 549 participants sustained an incident fall. These occurred in 65 respondents who had sustained frailty remission (Waves 1–3), 179 respondents who remained robust (Waves 1–3) and 381 respondents who remained frail over the three waves. The proportion of participants who experienced a fall during follow up was highest among those who remained frail (55.5%) and lowest among those who remained robust (12%), whereas among those who sustained frailty remission about one in six experienced a fall (16.7%).

The Kaplan Meier curve for occurrence of falls in those who had sustained frailty remission and those who were either robust or frail during Waves 1–3 is shown in Figure 1.

After adjustment for gender, age, marital status, smoking status and wealth, respondents who had a sustained frailty remission had a lower risk of experiencing falls over a subsequent 10-year period compared with those who were persistently frail (HR 0.41; 95% CI = 0·36–0.45) (see Table 2). As might be expected, the risk of falls among respondents who remained robust was significantly less than for those who were frail (HR 0.49; 95% CI = 0·43–0·56).

Sensitivity analysis

We performed a sensitivity analysis comparing previously described groups (n = 2,564) to the remaining participants at baseline (n = 6,780): those who either improved or deteriorated from Wave 2 to Wave 3 and those who were pre-frail across three waves. In addition to the 2,564 participants,

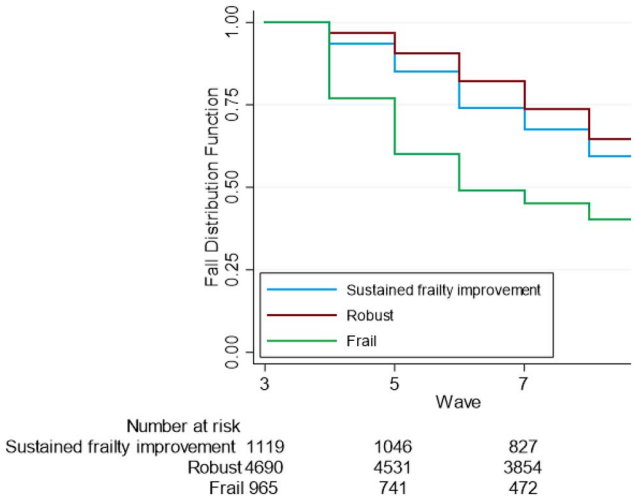

Figure 1. Occurrence of falls by the frailty category status (Waves 1–3): Kaplan Meier curves.

Table 2. Risk of falls (Waves 4–8) and frailty category status (Waves 1–3): Hazard ratio and 95% confidence intervals

Frailty category status	Hazard Ratio (95% CI)	*P*-value
Remain robust	0.49 (0.43, 0.56)	<0.0001
Sustained improvement in frailty	0.41 (0.36, 0.45)	<0.0001
Remain frail	1	Reference

Adjusted for covariates (gender, age, marital status, smoking status and wealth)

a further 2,000 remained pre-frail, 1,803 deteriorated and 2,977 improved in frailty status at the end of the study period (Waves 2–3). When the additional groups were added into the analysis, the lower risk of falls in those with frailty remission during Waves 1–3 compared with persistently frail participants persisted (HR = 0.43; 95%CI 0.39, 0.47) (see Supplementary Table 3). This was true also for risk of falls among those who remained robust compared with those with persistent frailty (HR = 0.43). Interestingly, there was a lower risk of falls in those who remained robust from Wave 1 to Wave 3 compared with those who improvement their frailty from Wave 2 to Wave 3 (an improvement over 1.5 years), which was marginally lower than that of the sustained frailty group. The risk of falls was marginally less in this group compared with those who improved their frailty from Wave 1 to Wave 3 (a sustained improvement).

Discussion

To our knowledge, this is the first study to assess using the frailty index, transitions in frailty status over a 5-year period and how sustained frailty remission is associated with risk of falls over a 10-year period. We found that 15.2% of older adults aged 50 years and older who were frail or pre-frail had an improved frailty status and sustained it over two follow-up visits. Our data confirms that frailty transitions are not unidirectional, but that they may be reversible and that among those whose frailty status improved, and the risk of falls was lower than those who remained frail.

There are limited prospective data assessing frailty remission and trends. Previous studies that have looked at frailty remission have used the frailty phenotype [13–15], a model that does not categorically include social and psychological dimensions, although these are implicitly included through its measures.

Gill and colleagues analysed data from 754 participants from the Precipitating Events Project with assessment of frailty using frailty phenotype at baseline, 18, 36 and 54 months. They found that despite it being less common, transitions to states of lesser frailty occurred [15]. Our data are consistent with these findings and extend them in a larger cohort using the frailty index as a measure of frailty status.

We found a slightly higher frequency of participants who improved their frailty status compared with Kojima and colleagues, who used frailty phenotype [13]. It is possible that these higher rates of change could be due to our use of the frailty index, where cumulation in socioeconomic factors and health determinants may have caused incremental changes in frailty to be more prominent [24]. Overall, our findings are generally consistent with results from prior studies using frailty phenotype. However, it can be difficult to compare these studies with fewer time points and variable duration of the follow-up study.

To our knowledge, our study is the first to examine association with outcome. We showed a lower risk of falls in people who sustain persistent frailty remission compared with those who remain frail. Interestingly, the occurrence of falls was similar to that of those who remained robust.

Risk factors for falls include muscle weakness, unsteady gait, confusion and predisposing medications [9]. Frailty is multifactorial, and includes functional, psychological, cognitive and physical deficits. It is possible that improvement in any one of these may reduce the occurrence of falls.

What are the potential implications of our findings? Our data confirm that a proportion of people (15%) develop sustained remission from frailty. We also show those who have improved their frailty status have a lower risk of falls. Although it must be noted these transitions in frailty observed could be spontaneous, our findings provide hope that targeting interventions may potentially help reverse frailty and reduce adverse outcomes though further research is needed. A number of interventions have been suggested, including lifestyle factors (diet, physical therapy), monitoring, vaccination, additional input at stressor events and rehabilitation as potential methods to prevent frailty [11]. Physical therapy, however, has been shown to be the only successful intervention to date [26, 27]. Gill and colleagues showed benefits from physical therapy in a moderate, though not severe, frailty group, which may suggest that reversibility is more difficult in those with greater frailty [25]. Further research needs to assess predictors for individuals to make improvements/decline in frailty status [28], and further analyse which interventions may

impact frailty remission and whether these changes measured outcomes such as falls risk.

The main strengths of our data include the relatively long-time scale over which data on frailty status and falls have been collected, enabling trends in frailty to be assessed at multiple time points and also the sampling designed to represent people aged 50 and over, living in private households in England.

There are, however, several limitations to be considered in interpreting the results. Although being population-based and the sample being drawn from across the UK, the proportion of participants from ethnic minority groups is relatively small (< 2%), limiting the generalisability of the data and requiring that we merge potentially heterogeneous ethnic groups. We cannot exclude the possibility of selection bias despite ELSA using multiple methods to aid study response. Data on falls were obtained by self-report and subject therefore to errors of recall and reporting bias; any misclassification, however, is likely to have resulted in a reduced chance of finding significant biological associations. In our analysis, we adjusted for a range of potential confounders; we cannot exclude either unknown or residual confounding as possible explanation for our findings. In our data, death was a potential competing risk. We were, however, not able to undertake a competing risk analysis as data on end of life in ELSA was only available in Waves 2, 3, 4 and 6, and data on mortality did not include all mortality cases in those waves [29].

There remain complexities assessing frailty over time, given its dynamic nature and the fact individuals can transition through multiple changes in frailty status. Where studies measure frailty at a given time point, the overall reflection of an individual's frailty status may not be accurate, for example, when an individual makes a short-term change in frailty status after a stressor event such as an acute physical health condition (e.g. myocardial infarction) or a procedure (e.g. surgery) [10]. We therefore cannot conclude that remission in frailty is what causes changes in falls risk. Future work could be performed using index falls risk to demonstrate changes and assess the impact of interventions shown to reduce frailty, on outcomes such as future falls. This study did not observe the impact of frailty trajectory on other important outcomes such as fragility fracture, which could be considered in future studies. Given that 5–6% of falls result in fractures [30], future studies would need to ensure adequate power to observe this.

In addition, by using cut-offs to determine frailty and pre-frailty, trends may not be correctly understood for individuals who are on the border of the two groups. Further research needs to focus on developing complex models to show individuals frailty trajectories allowing for short-term changes.

In conclusion, our data confirm that 15% of older people experience persistent and sustained improvement in frailty status over a 5-year period. Falls risk among these people is lower compared with those who remain frail. As the confidence intervals of the hazard ratios overlap between robust and those with persistent frailty remission it appears that their risk is a similar level as those who remain robust. This offers us opportunity to highlight the observed remission in frailty noted and guide future work accordingly: maintaining robust function is important, but so is reversing frailty.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

Declaration of Conflicts of Interest: None.

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Data Availability Statement: The data that support the findings of this study are openly available in ELSA at https://www.elsa-project.ac.uk/accessing-elsa-data.

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